not less than 90 percent nor more than 125 percent of the number of milligrams of gentamicin that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 3.0 nor more than 5.5. The gentamicin sulfate used conforms to the standards prescribed by § 444.20(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The gentamicin sulfate used in making the batch for potency, loss on drying, pH, specific rotation, content of gentamicins C_1,C_{1a},C_2, and identity.

(*b*) The batch for gentamicin potency, sterility, pyrogens, and pH.

(ii) Samples required:

(*a*) The gentamicin sulfate used in making the batch: 10 packages, each containing approximately 500 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 40 containers if each milliliter contains the equivalent of 2.0 milligrams or 10.0 milligrams of gentamicin; a minimum of 12 containers if each milliliter contains the equivalent of 40.0 milligrams of gentamicin; or, a minimum of 10 containers if each milliliter contains the equivalent of 1.0 milligram of gentamicin.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Using 0.1*M* potassium phosphate buffer, pH 8.0 (solution 3), dilute an accurately measured representative portion of the product to the reference concentration of 0.1 microgram of gentamicin per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) [Reserved]

(4) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter, except inject a sufficient volume of the undiluted solution to deliver 10 milligrams of gentamicin per kilogram, but not to exceed 10 milliliters per kilogram.

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

[39 FR 19046, May 30, 1974, as amended at 46 FR 2994, Jan. 13, 1981; 46 FR 16683, Mar. 13, 1981; 46 FR 31009, June 12, 1981; 47 FR 56490, Dec. 17, 1982; 48 FR 44775, Sept. 30, 1983; 49 FR 49287, Dec. 19, 1984; 50 FR 10754, Mar. 18, 1985; 50 FR 19919, May 13, 1985]

§ 444.230 Kanamycin sulfate injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Kanamycin sulfate injection is an aqueous solution of kanamycin sulfate with suitable and harmless buffer substances and preservatives. It contains either 75 milligrams of kanamycin per 2.0 milliliters, or 250 milligrams of kanamycin per milliliter, or 1.0 gram of kanamycin per 3.0 milliliters. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of kanamycin that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 3.5 and not more than 5.0. The kanamycin sulfate used conforms to the standards prescribed by § 444.30a(a)(1)(i), (v), (vii), (viii), (ix), and (x).

(2) *Labeling.* In addition to the requirements prescribed by § 432.5 of this chapter, the labeling of each package shall bear a warning to the effect that older patients and patients receiving a total dose of more than 20 grams of the drug should be carefully observed for signs of eighth-nerve damage. In patients with impaired kidney function or with prerenal azotemia, the risk of severe ototoxic reaction that may result in permanent deafness is sharply increased.

(3) *Requests for certification; samples.* In addition to the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The kanamycin sulfate used in making the batch for potency, residue on ignition, loss on drying, identity, crystallinity, and kanamycin B content.

(*b*) The batch for potency, sterility, pyrogens, and pH.

(ii) Samples required:

(*a*) The kanamycin sulfate used in making the batch: 10 packages, each containing approximately 500 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: Minimum of 12 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Place an accurately measured representative aliquot of the sample into an appropriate-sized volumetric flask and dilute to volume with sterile distilled water to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 10 micrograms of kanamycin per milliliter (estimated).

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) [Reserved]

(4) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 10 milligrams of kanamycin per milliliter.

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

[39 FR 19046, May 30, 1974, as amended at 50 FR 19919, May 13, 1985]

§ 444.246 Netilmicin sulfate injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Netilmicin sulfate injection is an aqueous solution of netilmicin sulfate and one or more buffers, chelating agents, antioxidants, and preservatives. Each milliliter contains netilmicin sulfate equivalent to 10 milligrams, 25 milligrams, or 100 milligrams of netilmicin. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of netilmicin that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 3.5 and not more than 6.0. The netilmicin sulfate used conforms to the standards prescribed by § 444.46(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The netilmicin sulfate used in making the batch for potency, loss on drying, pH, residue on ignition, specific rotation, and identity.

(*b*) The batch for potency, sterility, pyrogens, and pH.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(*a*) The netilmicin sulfate used in making the batch: 12 packages, each containing approximately 500 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 12 immediate containers.

(*2*) For sterility testing: 20 immediate containers collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dilute an accurately measured representative portion of the product with 0.1*M* potassium phosphate buffer, pH 8.0 (solution 3), to the reference concentration of 0.1 microgram of netilmicin per milliliter (estimated).

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter, using a solution containing 10 milligrams of netilmicin per milliliter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

[48 FR 18801, Apr. 26, 1983, as amended at 55 FR 11584, Mar. 29, 1990]

§ 444.262 Sisomicin sulfate injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Sisomicin sulfate injection is an aqueous solution of sisomicin sulfate and one or more suitable buffers, chelating agents, and preservatives.